INSTRUCTOR'S GUIDE

FREEDOM FROM UNACCEPTABLE RISK: MAKING A CASE FOR SAFETY ASSURANCE AND RISK MANAGEMENT

LEARNING OBJECTIVES

1. To review the regulatory background of the safety assurance case
2. To identify fundamental concepts of safety assurance for medical devices
3. To explore how a risk management framework may support a safety assurance case
4. To apply the framework of risk assessment and risk control to an infusion device

TOPICS

Safety assurance; risk management; regulatory basis for safety assurance

ASSUMPTIONS

The case study is based on the following assumptions:

- Target audience is undergraduate/graduate students who have no experience in the medical device industry.
- Users of the case study are instructors who have some basic knowledge of the U.S. Food and Drug Administration.
- Instructors may spend 2–4 hours to teach the material, including student presentations.

Instructors should—

- Be familiar with the reference materials listed
- Dedicate sufficient preparation time for class lecture
- Instruct students to be prepared at least 2 weeks before class
- Prepare, engage, and immerse students in the lessons learned from the case study

SUGGESTED APPROACH

1. Preparing Students (Before Class): Students are expected to read the case study and other materials and complete assigned activities before class.
2. Engaging Students (In Class): This session is a lecture on how risk management could apply to the safety assurance case and a discussion of infusion devices.
3. Immersing Students (After Class): This is a team project that demonstrates understanding of a safety assurance case and risk management activities for an infusion device.e.

STUDENT ACTIVITIES

BEFORE CLASS

I. Review the following materials:

1. Using External Infusion Pumps Safely: FDA Patient Safety News, Show #100, July 2010

   http://www.accessdata.fda.gov/psn/printer.cfm?id=1329

2. Infusing Patients Safely: Priority Issues From the AAMI/FDA Infusion Device Summit

   http://www.aami.org/publications/summits/AAMI_FDA_Summit_Report.pdf

3. Code of Federal Regulations, Title 21, Parts 860, 807, and 820

   http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm

4. Application of Risk Management to Medical Devices Standard (ISO 14971; to be provided)

II. Answer the following questions:

1. What an infusion pump?
2. List the eight categories of hazards suggested by FDA.
3. List three hazards in each category.
4. What are the definitions of the following terms according to ISO 14971?
   - Safety
   - Risk
   - Harm
   - Hazard
   - Hazardous situation
5. What are the supportive regulatory requirements to do a safety assurance case report?

III. References:

Note: Draft guidances are subject to change and are not for implementation.

1. U.S. Food and Drug Administration: Factors To Consider When Making Benefit-Risk Determination in Medical Device Premarket Approval and De Novo Classification, March 28, 2012

   http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM296379.pdf

2. U.S. Food and Drug Administration: Infusion Pump Improvement Initiative, April 2010

   http://www.fda.gov/downloads/MedicalDevices/ProductsandMedicalProcedures/GeneralHospitalDevicesandSupplies/InfusionPumps/UCM206189.pdf

3. Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions Draft Guidance, April 23, 2010

   http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM209337.pdf

IN CLASS

I. Questions for small group discussion:

1. What are the differences between risk assessment and risk management?
2. What are the steps to do a comprehensive risk assessment?
3. How do you build a comprehensive risk management system?

AFTER CLASS

I. Team Project

1. Review the following two video clips from FDA Patient Safety News:
   a. Safety Information on Alaris SE Infusion Pumps, Show #57, November 2006

      http://www.accessdata.fda.gov/psn/printer.cfm?id=471

   b. Baxter Infusion Pumps Recalled Because of Service Error, Show #68, October 2007

      http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/psn/printer.cfm?id=563

2. Select one of the "to be determined" sublevel 2 claims from the safety case diagram on page 6 and collect publicly available information and data to formulate a risk assessment that follows the process discussed in class. Complete and discuss the short circuit claim as follows:
   a. Claim: Power surge hazards are mitigated.
   b. Definition: Power surge may refer to Voltage Spike, Current Spike, or Transferred Energy Spikes.
   c. Subclaim 1: Power surge hazards are prevented.
   d. Evidence: to be developed.
   e. Subclaim 2. Power surge hazards are detected.
   f. Evidence: to be developed.
   g. Subclaim 3: Power surge hazards are mitigated.
   h. Subclaim 3.1: Fuses are implemented to mitigate power surge hazards.
   i. Evidence: Adequate design requirements exist for fuses.
   j. Evidence: V/V testing demonstrate fuses adequately protect against worst case power surge of X Joules.
3. Present your risk management results in a safety assurance case report format.

Note: This case study may be used to as a part of academic requirements such as a thesis, senior project, or graduate project.

RECOMMENDED READINGS

Note: Draft guidances are subject to change and are not for implementation.

1. Arney, D.E., Jetley, R., Jones, P., Lee, I., Ray, A., Sokolsky, O., & Zhang, Y. (2009). Generic Infusion Pump Hazard Analysis and Safety Requirements, Version 1.0. Technical Report. Philadelphia: University of Pennsylvania.

   http://repository.upenn.edu/cis_reports/893/

2. Flick, G.J., Salyer, J., et al. (2008). Medical Product Risk Management Training Using HACCP Principles (4th ed.). Medical HACCP Alliance: Blacksburg, VA.

   http://globalriskmanagementalliance.com/merchandise.shtml

3. Hawkins, R., Kelly, T., Knight, J., & Graydon, P. (2011). A New Approach to Creating Clear Safety Arguments. Southampton, England: Safety-Critical Systems Symposium.

   http://www.cs.virginia.edu/~jck/publications/SSS.2011.safety.cases.pdf

4. Leveson, N.G. (2011). The use of safety cases in certification and regulation. Journal of System Safety, 47(6).

   http://sunnyday.mit.edu/SafetyCases.pdf

5. Risk Management—Risk Assessment Techniques. (2009). IEC/ISO 31010.

   http://webstore.iec.ch/preview/info_ieciso31010%7Bed1.0%7Db.pdf

6. Safety Aspects—Guidelines for Their Inclusion in Standards. (1999). ISO/IEC Guide 51.

   http://www.iso.org/iso/home/store/catalogue_tc/catalogue_detail.htm?csnumber=32893

7. Total Product Life Cycle: Infusion Pump—Premarket Notification [510(k)] Submissions Draft Guidance, April 23, 2010.

   http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM209337.pdf

8. Toulmin, S.E. (1958). The Uses of Argument. Cambridge, England: Cambridge University Press.

9. Weinstock, C.B., & Goodenough, J.B. (2009). Towards an Assurance Case Practice for Medical Devices. Technical Note CMU/SEI-2009-TN-018. Software Engineering Institute.

   http://www.sei.cmu.edu/reports/09tn018.pdf

SUPPLEMENTARY MATERIALS

SAFETY ASSURANCE CASE, RISK ASSESSMENT, AND HAZARDS

A safety assurance case gathers its inputs from the documented activities and results of the system risk assessments, controls, and associated benefit-risk determinations. The case is a living document containing all risk management activities that facilitate how hazards and associated hazardous situations are controlled or mitigated, resulting in freedom from unacceptable risk. Thus, risk management activities provide evidence to support the safety arguments that summarize and justify the claim that the system is reasonably safe.

The central part of a safety case is the identification, assessment, and management of hazards. The hazard log or list is one of the most important tools for managing safety. A hazard is a set of conditions in the operation of a product with the potential for initiating or contributing to events that could result in injury to people, damage to property, or harm to the environment.

Hazards are properties or states of an entire system or medical device and may be defined at any level. It is essential to select the right level. A common fault is to select it too low, resulting in too many hazards, no system properties, being expensive or impossible to track, and overengineering. If the level is selected too high, it is difficult to ensure comprehensive management. For medical device hazards, it may be beneficial to select hazard levels as the outputs that could initiate harm to people, property, or the environment.

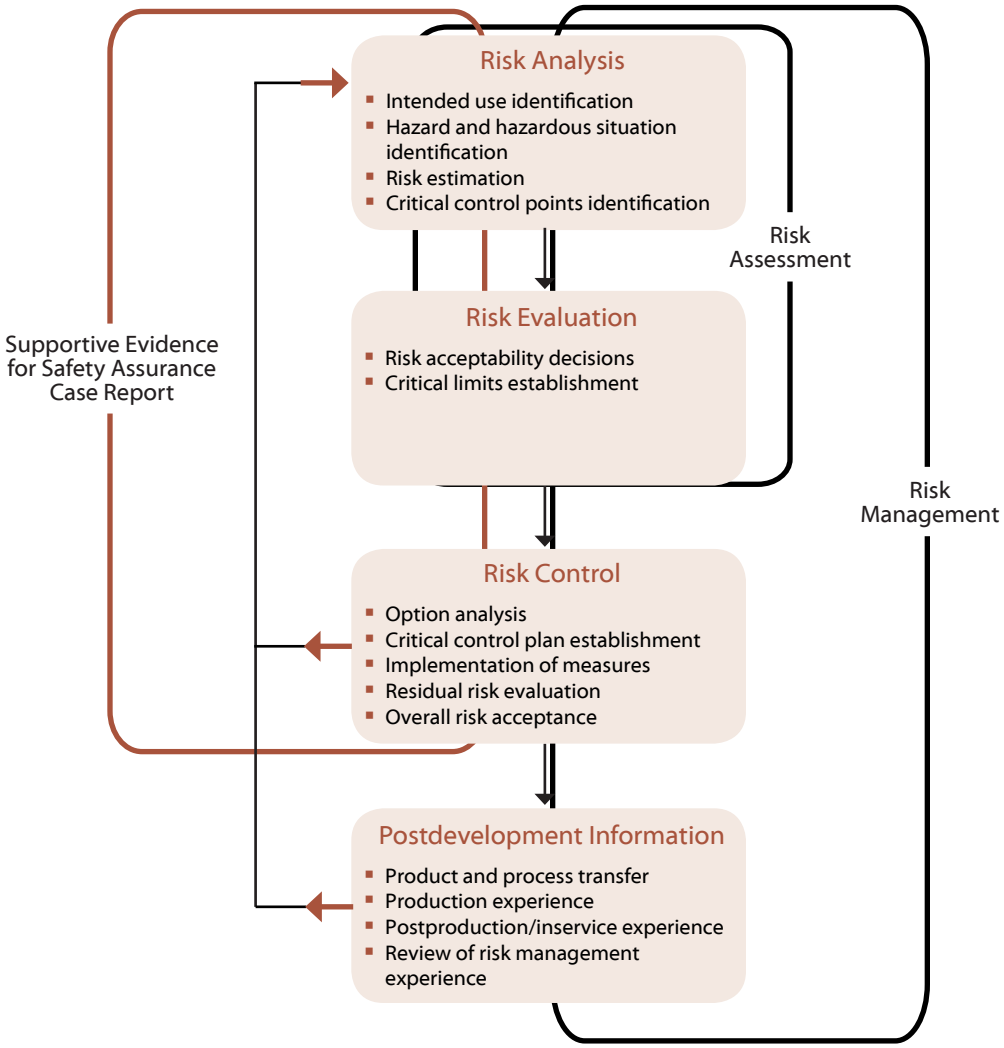
GUIDELINE FOR RISK ASSESSMENT AND RISK MITIGATION

A risk management process (see figure, next page) should be integrated into the quality management system for a medical device. The tasks of analyzing, evaluating, and controlling or mitigating risk provide evidence to support the safety assurance case.

Analyze Risk

Safety assurance includes essential steps for conducting hazard analysis and determining critical control points. The product's requirements must be documented in terms of marketing, performance, function, regulations, legal concerns, etc. This information provides a firm

Risk Management Framework



foundation for the development team engaged in risk management planning and implementation. The team then analyzes and records the intended use and purpose of the device, which defines the scope for risk assessment. For example, the risks associated with home use are different from those associated with hospital use. The indication for use, such as the application environment, clinical purpose, organs or systems affected, and profiles of patient and user, forms the basis to initiate hazard identification and carry out further risk management activities.

Once a hazard is identified, the development team assesses the severity of harm and probability of occurrence of that harm caused by the hazard and its associated hazardous situation(s). For example, overdelivery of insulin is a hazard of an insulin infusion device. Insulin overdose causes serious injury (harm)—hypoglycemia, or low blood sugar—to a diabetic patient. The team then estimates the probability that the harm would occur.

Evaluate Risk

If a hazard poses a risk level that is of safety concern, the development team should identify critical control measures. For example, the amount of insulin infused is a safety concern to a diabetic patient.

Therefore, the infusing mechanisms that control the rate and time of insulin delivery are the critical control points. These mechanisms are points of significant interest to be designed properly and monitored continuously.

After determining critical control points, the team establishes critical limits (e.g., infuse rate of X+z ml/seconds for a duration of Y+0.1 seconds) and procedures to continue monitoring those parameters. Then the team determines the acceptability of that risk after the implementation of the critical control points. Consequently, the team undertakes actions depending on the level of risk for each issue identified.

Mitigate or Control Risk

ISO's risk management standard is very specific about how risk should be controlled. It stipulates an option analysis (clause 6.2) that requires prioritization when planning risk control measures. The measures should be considered in the following order:

1. Inherent safety by design (the preferred risk control measure)
2. Protective measures in the product or manufacturing process
3. Information for safety (the last resort risk control measure)

The development team ensures implementation of these risk control measures and demonstrates their effectiveness. The team records objective evidence of implementation and effectiveness of the measures in the device risk management report or the safety assurance case report.

In practice, risk analysis, risk evaluation, and risk control are iterative processes. The applications of critical control points are to effectively control individual risks within acceptable levels. The team continues this process until the residual risk of each individual hazard is judged acceptable. Then the team conducts a review of the overall residual risk, i.e., the accumulation of all residual risks posed by each individual hazard after effective control measure(s) are applied. Finally, the team gathers and reviews data and literature on the medical benefits of the intended purpose and use of the device to determine whether the benefits outweigh the risk. The team then finalizes the device risk management report or safety assurance case report and determines whether a product is safe for use.